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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/164,764	10/01/98	SIDRANSKY	D 01107.76459

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EXAMINER	
SOUAYA, I	
ART UNIT	**PAPER NUMBER**
1655	17

DATE MAILED:
02/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File Copy

Office Action Summary

Application No.	Applicant(s)
09/164,764	Sidransky
Examiner	**Group Art Unit**
Jehanne Souaya	1655

☒ Responsive to communication(s) filed on *May 31, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *23-34* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *23-34* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☒ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Currently, claims 23-34 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The request for reconsideration after final rejection has been entered and prosecution has been reopened in the present application. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), *at the time the application was filed*, had possession of the claimed invention.

The claims as written are inclusive of methods for detecting any cancer by detecting a microsatellite length alteration in a DNA sample from a bodily fluid from a patient wherein the sample is obtained from blood, urine, sputum, bile, stool, cervical smears, saliva, tears, cerebral spinal fluid, and lymph nodes. The specification teaches detecting bladder cancer comprising detecting variations in the microsatellite markers ARA, AR, MD, SAT, ACTBB2, FGA, and UT762 in urine verses a normal control specimen (example 3); detecting Small Cell Lung Cancer comprising detecting variations in the microsatellite markers AR, ACTBB2, and UT762 in sputum verses a normal control specimen; detecting Non Small Cell Lung Cancer comprising detecting variations in microsatellite markers ARA, D14S50, AR, MD, SAT, ACTBB2, FGA, and UT762 in sputum versus a normal control specimen, detecting head and neck small cell carcinoma comprising detecting variations in the microsatellite markers ARA, D14S50, AR, SAT, DRPLA, ACTBB2, and FGA in head and neck specimens versus a normal control specimen (table 1). However, it is highly unpredictable as to whether additional cancers can be detected by analyzing other biological fluids because it is unpredictable as to whether other types of biological fluids contain cancer cells. All organs drain blood, for example. There is no evidence in the specification that any type of tumor cell or tumor DNA is present in blood, lymph node fluid, or tears, for example, at a ratio to normal cells or normal cell DNA that would allow for the accurate detection of alterations in the microsatellite DNA of any tumor cell. Furthermore, the specification does not

provide evidence that cells from any other type of cancer would be expected to be present in biological fluids at levels sufficient to allow for the specific detection of microsatellite variations from cells of the cancer. For example, Table 1 presents data demonstrating the correlation of specific loci to different types of cancer, SCC, NSCLC, SCLC, and TCC. In each evaluation, there is between a 60% and 100% non- correlation of an alteration of any one of these loci with any one of the above identified neoplasms. Therefore, where the occurrence of a mutation in a given allele does not positively correlate to a neoplasm beyond that of random chance, the skilled artisan would not be able to discriminate between those rare instances where cancer cells are present as opposed to where cancer cells are not present in the specimen taken from a site remote to a primary neoplasm.

The claims encompass a broad genus. That is, the claims encompass detecting any cancer, ie: Ewing's Sarcoma, Osteosarcoma, Brain Stem Glioma, Cerebellar Astrocytoma, Cerebral Astrocytoma, Ependymoma, Medulloblastoma, Supratentorial Primitive Neuroectodermal and Pineal Tumors, Visual Pathway and Hypothalamic Glioma, Breast Cancer, Cerebellar Astrocytoma, Cerebral Astrocytoma, Medulloblastoma, Supratentorial Primitive Neuroectodermal Tumor, Hodgkin's Disease, Acute Lymphoblastic Leukemia, Acute Myelocytic Leukemia, Liver Cancer, Neuroblastoma, Non-Hodgkin's Lymphoma, Retinoblastoma, Rhabdomyosarcoma, Soft Tissue Sarcoma, Anal Cancer, Esophageal Cancer, Gallbladder Cancer, Liver Cancer, Pancreatic Cancer, Small Intestine Cancer, Adrenocortical Carcinoma, Parathyroid , Pituitary Tumor, Thyroid Cancer, Kidney (Renal Cell) Cancer, Penile Cancer, Prostate Cancer, Testicular Cancer,

Renal Pelvis and Ureter Cancer, Cervical Cancer, Endometrial Cancer, Ovarian Epithelial Cancer, Uterine Sarcoma, Vaginal Cancer, Acute Myeloid Leukemia (AML), Chronic Lymphocytic Leukemia (CLL), Chronic Myelogenous Leukemia (CML), Cutaneous T-Cell Lymphoma, Primary Central Nervous System Lymphoma, Rhabdomyosarcoma, Melanoma, Islet Cell Carcinoma, by detecting any microsatellite instability (encompasses unknown microsatellite markers) in any bodily fluid draining the organ, ie: blood, urine, sputum, bile, stool, cervical smears, saliva, tears, cerebral spinal fluid, and lymph nodes. Each of the claimed inventions is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filling date applicant was in possession of the claimed invention. In the instant case, the state of the art of diagnosing cancer by analyzing biological fluids is highly unpredictable The ability to detect microsatellite variations in DNA samples obtained from biological fluids requires that the biological fluid contains cancer cells or cancer cell DNA. The specification as filed does not support the full scope of the claims because the specification has not provided sufficient guidance to enable the skilled artisan to diagnose any type of cancer by detecting the presence of cancer cell or cancer cell DNA. Given the lack of guidance provided in the specification, the specification fails to show that applicant was in fact "in possession of the claimed invention" at the time the application for patent was filed.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 23-34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-9, 12-18, and 20-25 of copending Application No. 08/968,733. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are inclusive of methods for detecting a cell proliferative disorder comprising detecting an allelic imbalance at a genetic locus

which comprises microsatellite DNA wherein the test sample is selected from the group consisting of urine, sputum, bile, stool, saliva, tears, serum, and plasma.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 23-34 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,2,4,6,8,17,18,22-25,28,29,31, and 35 of copending Application No. 09/038,637. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of the '637 are inclusive of methods for detecting cancer by detecting genetic instability, including genetic instability at a microsatellite allele of a patient compared to a control specimen wherein the microsatellite DNA is obtained from a saliva specimen.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

2/13/01